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Quantitation of Regional Cerebral Blood Flow Increases During Motor Activation: A Multislice, Steady-State, Arterial Spin Tagging Study

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Steady-state arterial spin tagging approaches were used to construct multislice images of relative cerebral blood flow changes during finger-tapping tasks. Statistically significant increases in cerebral blood flow were observed in primary sensorimotor cortex in all seven subjects. The mean volume of the activated region in the contralateral primary sensorimotor cortex was 0.9 cm^3, and the mean increase in cerebral blood flow in the activated area was 54% ± 11%. Although the extended spatial coverage is advantageous for activation studies, the intrinsic sensitivity of the multislice approach is smaller than the intrinsic sensitivity of the single-slice, arterial spin tagging approach. Magn Reson Med 42:404–407, 1999. Published 1999 Wiley-Liss, Inc.†

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Steady-state arterial spin tagging approaches (1,2) can give quantitative images of cerebral blood flow in humans (3–6) and have been validated against $H_2{}^{15}O$ positron emission tomography (PET) techniques (7). An important application of arterial spin tagging approaches is the study of regional cerebral activation. For example, steady-state arterial spin tagging approaches have been used to obtain single-slice images of cerebral blood flow increases in the primary sensorimotor cortex during motor tasks (8) and prefrontal cortex during cognitive tasks (9).

Single-slice imaging approaches are not optimal for activation studies because of the limited coverage of the brain. A multislice spin tagging approach recently has been reported (10), but the sensitivity is reduced compared with the single-slice approach. This decrease in sensitivity and the consequent decrease in statistical power could restrict the utility of multislice arterial spin tagging techniques for functional activation studies. The aim of the work presented here was to investigate whether multislice arterial spin tagging approaches could be used to measure statistically significant regional cerebral blood flow increases during motor activation paradigms.

MATERIALS AND METHODS

Experimental Protocol

Experiments were performed on seven normal, right-handed subjects (three males and four females) by using a protocol approved by the Institutional Review Board of the National Institute of Mental Health. The subject group was identical to the subject group used for a previous finger-tapping activation study (8).

Multislice images were acquired from a 45-mm slab that included the primary sensorimotor cortex (see Fig. 1). Steady-state spin tagging approaches (see below) were used to obtain 168 perfusion-weighted images from the nine slices in the slab over a 28-minute period. During this 28-minute period, subjects alternated between intervals of rest and intervals of finger tapping: Both the rest interval and the tapping interval were 120 sec long. Finger tapping involved self-paced sequential apposition of the fingers of the right hand against the right thumb at a frequency of ≈ 2 Hz.

MR Imaging

All experiments were performed on a Signa 1.5 T scanner (General Electric, Milwaukee, WI) using a standard quadrature head coil and a standard body-gradient coil capable of a maximum amplitude of 22 mT/m and a maximum slew rate of 120 T/m/sec. Anatomical images were acquired by using an SPGR sequence with a matrix of 256 × 256 and a slice thickness of 5 mm (TE, 4 msec; TR, 33 msec; flip angle, 45°).

Multislice gradient echo SPIRAL techniques (11,12) were used to obtain a series of nine two-dimensional, axial interleaved images covering the 45-mm slab. The field of view in the z direction could have been increased to 75 mm (15 slices), but this more extensive coverage was not required for the motor experiments reported here. Each two-dimensional image was obtained by using a matrix of 64 × 64; field of view, 24 cm; slice thickness, 5 mm; and TE, 4 msec. The length of the SPIRAL waveform used to encode the data for each slice was 22 msec: A complete multislice data set was acquired in 270 msec (TR, 5 sec). Image registration (13) was used to correct for head motion, and the central seven slices were used for further analysis.

Spin Tagging

Flow-induced adiabatic inversion (2) was used to invert arterial water spins flowing through the ‘‘tagging’’ plane,

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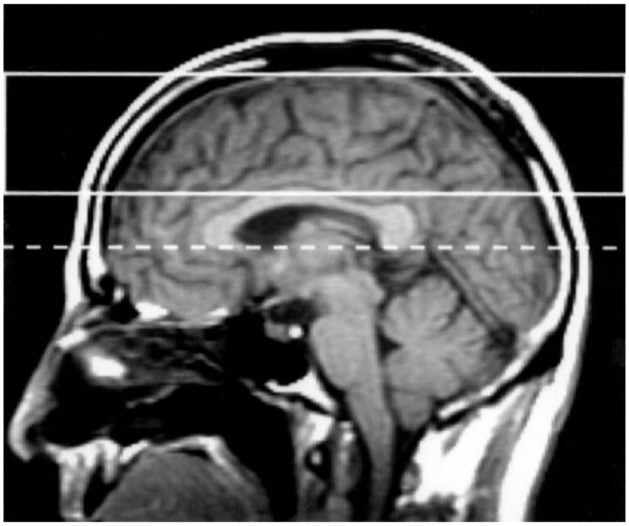

FIG. 1. Sagittal image of the human head showing the approximate location of the imaging slab (solid lines) and the inversion plane (dashed lines) used for the perfusion experiment.

which was placed approximately 2 cm below the proximal edge of the slab (Fig. 1). Details of the inversion pulse train have been described previously (8). The frequency off-set of the inversion pulses varied from 5 kHz to 14 kHz, depending on the slice. In the ''control'' scan, the off-resonance radiofrequency amplitude was modulated sinusoidally (at 125 Hz) to reduce arterial tagging and control for magnetization transfer effects (10). The ''control'' scan was subtracted from the ''tagged'' scan to construct the ΔM image.

Arterial spin tagging data were acquired by using a ''delayed acquisition'' approach (5). In this approach, a delay (τ_{delay}) was inserted between the end of the tagging period and the beginning of the acquisition of the SPIRAL image for the slab. τ_{delay} ranged from 1.1 sec to 1.3 sec, depending on the position of the slice. The ΔM values for the longer τ_{delay} values will be slightly smaller (≈12%) than the ΔM values for the shorter τ_{delay} value (F.Q. Ye, unpublished data), resulting in a slightly smaller statistical power for these slices.

Processing of ΔM Images

The voxel size of the 64 × 64, two-dimensional $\Delta M/M_o$ images was 3.75 mm × 3.75 mm. ΔM images were interpolated with zeros from 64 × 64 to 256 × 256 and convolved with a two-dimensional Gaussian kernel having a full width at half maximum (FWHM) of 5.6 mm. A ''dummy'' scan was inserted at the beginning of the sequence to minimize saturation effects. All of the ΔM images obtained under ''rest'' conditions were averaged together, and all of the ΔM images obtained under ''finger-tapping'' conditions were averaged together. A ΔM ''difference'' image was calculated by subtracting these two images, and ''t'' scores were calculated by using standard statistical procedures (8,9).

The threshold for statistical significance in the t images (t_{crit}), was calculated by correcting the image-based *P* value to obtain a voxel-based *P* value. A single-sided test was used. The voxel-based *P* value was calculated by using the Bonferroni correction, i.e., by dividing the image-based *P* value by the total number of brain voxels in the original slab. The average number of brain voxels in the slab was 5035 ± 760 voxels.

RESULTS

Relative Changes in Cerebral Blood Flow on Activation

ΔM difference images were constructed by subtracting the ΔM image obtained under control conditions from the ΔM image obtained under finger-tapping conditions. A critical t value for statistical significant changes in ΔM during finger tapping, t_{crit}, was calculated by using a *P* value of 0.1 for the entire slab and a Bonferroni correction for the number of brain voxels in the slab (see Materials and Methods). The average value of t_{crit} for the seven subjects was 4.2 ± 0.04.

Cerebral blood flow values are directly proportional to ΔM (1,2,5). Thus, activated regions of the cerebral blood flow image correspond to activated regions of the ΔM image, and relative changes in cerebral blood flow during activation will be equal to relative changes observed in ΔM (see below).

An example of a cerebral blood flow ''activation'' image is shown in Figure 2. For this individual, activation was observed in both the primary sensorimotor cortex and the supplementary motor area. Activation in the primary sensorimotor cortex extended through a number of axial slices, although activation in the supplementary motor area essentially was confined to one slice.

Relative changes in cerebral blood flow are summarized in Table 1 for all seven subjects. All subjects showed activation in the primary sensorimotor cortex, and, in all of these subjects, the activation extended through a number of slices. The mean volume of the activated primary sensorimotor cortex region was 900 mm^3, whereas the mean increase in cerebral blood flow in the activated region was 54% ± 11%. In addition, two subjects showed activation in the supplementary motor area. The mean volume of the activated supplementary motor area in these two subjects was 125 mm^3, and the mean increase in cerebral blood flow in the activated region was 55% ± 19%.

DISCUSSION

Finger-tapping paradigms would be expected to increase cerebral blood flow in the contralateral primary sensorimotor cortex and the supplementary motor area (14). All of the subjects showed statistically significant increases in cerebral blood flow in primary sensorimotor cortex during a finger-tapping task (see Table 1). The average increase in cerebral blood flow in the activated primary sensorimotor cortex regions (54% ± 11%) was similar to the average increase in regional cerebral blood flow observed with the same group of control subjects (63% ± 22%) using single-slice, arterial spin tagging techniques (8). If the differences in point-spread functions are taken into account (8), then the relative increases in cerebral blood flow in the primary sensorimotor cortex observed using arterial spin tagging approaches are consistent with the relative increases in cerebral blood flow observed using ^{133}Xe (14) and PET (15–17) approaches.

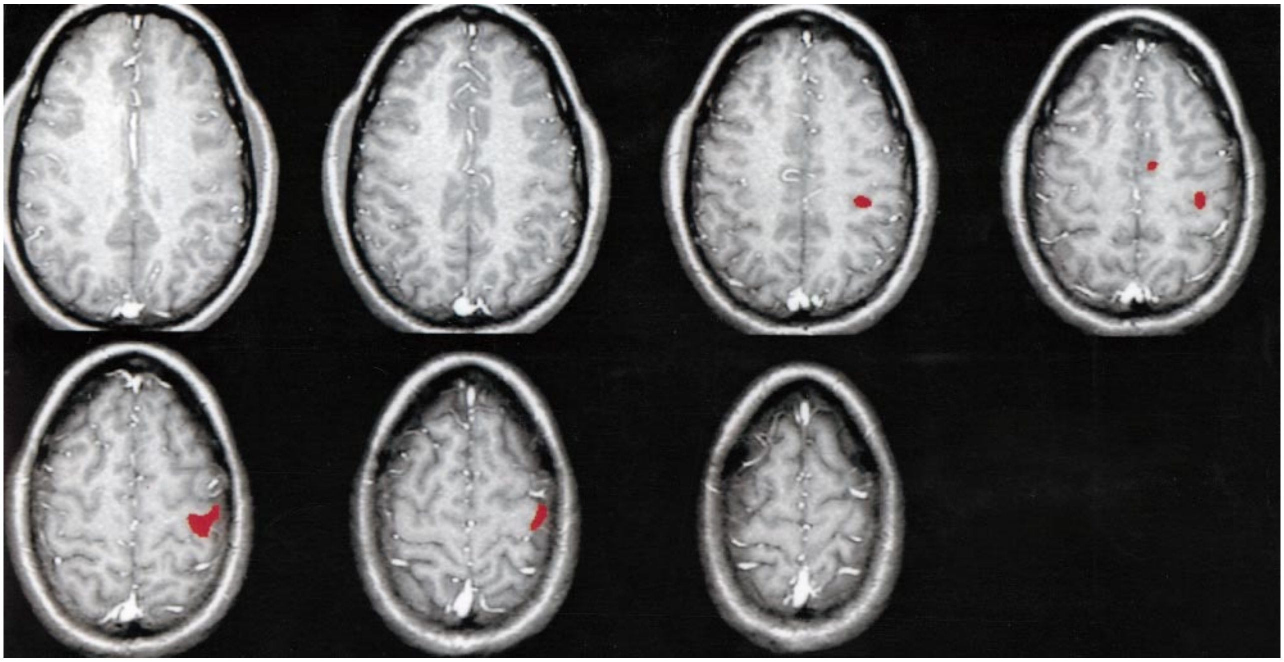

FIG. 2. Multislice finger-tapping activation images. Regions shown in red had statistically significant increases in ΔM during finger tapping. Data from subject 1.

Only two of the seven subjects showed statistically significant increases in cerebral blood flow in the supplementary motor area (see Table 1). However, five of the seven subjects showed statistically significant increases in cerebral blood flow in the supplementary motor area in single-slice, arterial spin tagging studies using a similar finger-tapping protocol (8). One reason for the reduced sensitivity in detecting activation in the supplementary motor area is the lower statistical power due to the smaller effective value of α (10).

Estimating changes by using suprathreshold pixels may have caused overestimation of blood flow changes in these experiments. However, such overestimates do not necessarily reduce the usefulness of this method for detecting brain activation.

We conclude that multislice arterial spin tagging approaches can detect statistically significant relative and absolute changes in cerebral blood flow in primary sensorimotor cortex during motor tasks. Although the wider spatial coverage of the multislice maps is advantageous for activation studies, the intrinsic sensitivity of the multislice approach is reduced compared with the sensitivity of single-slice, arterial spin tagging approaches.

Table 1
Average Volume and Relative Cerebral Blood Flow Increase of Activated Contralateral Primary Sensorimotor Cortex and Activated Supplementary Motor Area Regions

Subject	PSM		SMA	
	Volume (cm^3)[a]	ΔCBF (%)[b]	Volume (cm^3)[a]	ΔCBF (%)[b]
1	1.56	61.4	0.11	41.7
2	1.69	69.3	0.14	68.7
3	0.72	44.5	—	—
4	0.55	40.8	—	—
5	0.78	45.6	—	—
6	0.43	60.6	—	—
7	0.56	56.6	—	—

[a]Volume of the region with a statistically significant increase in cerebral blood flow during the finger tapping task.
[b]Average cerebral blood flow increase in the activated area. PSM, primary sensorimotor cortex; SMA, supplementary motor area; ΔCBF, relative cerebral blood flow increase.

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